

RESPIRATORY SYNCYTIAL VIRUS VACCINES EXPRESSING PROTECTIVE ANTIGENS FROM PROMOTOR-PROXIMAL GENES

ABSTRACT OF THE DISCLOSURE

Recombinant respiratory syncytial virus (RSV) having the position of genes shifted within the genome or antigenome of the recombinant virus are infectious and attenuated in humans and other mammals. Gene shifted RSV are constructed by insertion, deletion or rearrangement of genes or genome segments within the recombinant genome or antigenome and are useful in vaccine formulations for eliciting an anti-RSV immune response. Also provided are isolated polynucleotide molecules and vectors incorporating a recombinant RSV genome or antigenome wherein a gene or gene segment is shifted to a more promoter-proximal or promoter-distal position within the genome or antigenome compared to a wild type position of the gene in the RSV gene map. Shifting the position of genes in this manner provides for a selected increase or decrease in expression of the gene, depending on the nature and degree of the positional shift. In one embodiment, RSV glycoproteins are upregulated by shifting one or more glycoprotein-encoding genes to a more promoter-proximal position. Genes of interest for manipulation to create gene position-shifted RSV include any of the NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G genes or a genome segment that may be part of a gene or extragenic. A variety of additional mutations and nucleotide modifications are provided within the gene position-shifted RSV of the invention to yield desired phenotypic and structural effects.

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